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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/226,766	01/06/1999	LAWRENCE J. WANGH	08609/003004	9579

30623 7590 04/03/2003

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EXAMINER

CROUCH, DEBORAH

ART UNIT PAPER NUMBER

1632

DATE MAILED: 04/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/226,766

Applicant(s)

WANGH, LAWRENCE J.

Examiner

Deborah Crouch, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 142-163 is/are pending in the application.
- 4a) Of the above claim(s) 142-156 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 157-163 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 January 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 24, 2003 has been entered.

Claims 142-163 are pending. Claims 142-156 are withdrawn from prosecution as being to a non-elected invention. Newly added claims 157-163 are examined in this office action. The Declaration by Alexander D. Baguisi has been considered but is not fully persuasive for reasons presented below.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims s 157-161 and 163 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 5,480,772. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or

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would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are generic to claims 1-5 of '772.

Claims 157-161 and 163 are drawn to methods for reprogramming a non-dividing cell nucleus comprising contacting said nucleus with a CSF containing MII cell cytoplasm, and a method for in vitro activation of a non-dividing nucleus comprising providing a somatic cell nucleus, treating the nucleus with CSF cytoplasm and activating egg cytoplasm. Claims 1-5 of '772 are drawn to in vitro activation of human fetal red blood cell nucleus or a fetal cell found in amniotic fluid comprising isolating the nucleus from the cell and pretreating the nucleus with a non-ionic detergent, contacting the nucleus with CSF cytoplasm and with activating egg cytoplasm. The present claims are obvious over those of '772 because human fetal blood cells and cells found in amniotic fluid are non-dividing, and these cells are defined in the present specification as useful in the presently claimed method. Further each claim limitation in '772 can be found in the present specification, and thus is defined by "comprising" the present claims. Thus at the time of the present invention, it would have been obvious to the ordinary artisan to make the invention of present claims 157-161 and 163 given claims 1-5 of '772. Applicant is reminded that the preamble does not alter the obviousness when the method steps are the same or when the method claims are generic to the allowed claims.

Claims s 157-161 and 163 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 5,651,992. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably

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distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are generic to claims 1-14 of '992.

Claims 157-161 and 163 are drawn to methods for reprogramming a non-dividing cell nucleus comprising contacting said nucleus with a CSF containing MII cell cytoplasm, and a method for in vitro activation of a non-dividing nucleus comprising providing a somatic cell nucleus, treating the nucleus with CSF cytoplasm and activating egg cytoplasm. Claims 1-14 are drawn to a method for in vitro activation of a nucleus from a human fetal cell comprising separating the nucleus from the cell and contacting the nucleus with an activating egg extract. Fetal cells, as well as the specific cells claimed in claims 2 and 3, are all non-dividing cells as presently claimed, and are defined by the specification as claimed to be used in the invention of claims 157-161 and 163. Further, the use of a detergent, the specific detergent, activating under conditions where the cells do not synthesize nucleic acids as well as the activating egg extract being from *Xenopus* eggs are all contained in the present specification as definitions of the claimed invention. Thus, at the time of the present invention, it would have been obvious to the ordinary artisan to make the invention of present claims 157-161 and 163 given the claims 1-14 of '992. Applicant is reminded that the preamble does not alter the obviousness when the method steps are the same or when the method claims are generic to the allowed claims.

Claims 157-161 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 5,773,217. An obviousness-type double patenting rejection is appropriate where the conflicting claims

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are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are generic to claims 1-14 of '217.

Claims 157-161 are drawn to methods for reprogramming a non-dividing cell nucleus comprising contacting said nucleus with a CSF containing MII cell cytoplasm, and a method for in vitro activation of a non-dividing nucleus comprising providing a somatic cell nucleus, treating the nucleus with CSF cytoplasm and activating egg cytoplasm. Claims 1-29 of '217 are drawn to methods of activating sperm cells. Since sperm cells are non-dividing cells, the present claims are generic to claims 1-29 of '217. Each of the limitations found in claims 1-29 of '217 are defined in the present specification as elements to be used in the present claims given the use of "comprising." Thus, at the time of the present invention, it would have been obvious to the ordinary artisan to make the invention of present claims 157-161 given claims 1-29 of '217. Applicant is reminded that the preamble does not alter the obviousness when the method steps are the same or when the method claims are generic to the allowed claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 157-161 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of activating a non-dividing nucleus

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comprising isolating a nucleus, permeablizing the nucleus, incubating the nucleus with cytoplasm of an metaphase II oocyte, where the oocyte is from the same species as the nucleus, and incubating the nucleus with an activating egg cytoplasm, where the egg is from the same species as the nucleus, wherein said nucleus undergoes swelling, nucleic acid replication and entry into mitosis, does not reasonably provide enablement for any cell in metaphase II, where the nucleus, the cytoplasm and recipient egg are of different species, and activation without incubation with activating egg cytoplasm. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 162 and 163 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a nuclear transfer embryo comprising isolating a nucleus, permeablizing the nucleus, incubating the nucleus with cytoplasm of an metaphase II oocyte, where the oocyte is from the same species as the nucleus, and incubating the nucleus with an activating egg cytoplasm, where the egg is from the same species as the nucleus, transplanting the activated nucleus into an enucleated egg of the same species as the nucleus to form a nuclear transfer embryo, and a method for the in vitro activation of a non-dividing nucleus comprising the steps of isolating a nucleus, pretreating the nucleus with cytoplasm of an metaphase II oocyte, where the oocyte is from the same species as the nucleus, and incubating the nucleus with an activating egg cytoplasm, where the egg is from the same species as the nucleus, wherein said nucleus is activated to undergo DNA replication, does not reasonably provide enablement for any cell in metaphase II, where the nucleus, the CSF and activating cytoplasm and recipient egg are of different species and activation without incubation with activating egg cytoplasm. The specification does not enable any person skilled in the art to

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which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In claim 157, the end result of the method, nuclear swelling, nucleic acid replication and entry into mitosis are events associated with activation (specification, at least at, page 3, lines 20-25 and page 5, lines 30-32). At the time of filing, reprogramming could only be assayed by the development of a cloned animal. The mechanism of reprogramming was not known and frequently reprogramming wasn't complete as nuclear transfer embryos did not always develop to term (page 76, col. 2, parag. 2, lines 12-14 and page 77, col. 2, parag. 1, lines 3-5). Morphological events or structural changes observed associated with reprogramming were not clearly known but were thought to include timing of cleavage, compaction and blastocoel formation and cell surface antigens (Kono, page 76, col. 2, parag. 2, lines 8-11 and parag. 3, lines 1 to page 77, line 1). Further, the subsequent incubation, in claim 158, of the nucleus in the presence of activating egg cytoplasm is critical to the activation method as activation is required to obtain nuclear swelling, nucleic acid replication and entry into mitosis. It appears that for the crucial elements of the CSF cytoplasm and the activating egg cytoplasm to enter the nucleus, the nucleus must first be permeablized, as the specification does not teach that the claimed method results in nuclear envelop breakdown, a requirement for exposure of the donor nuclei to MPF (Kono, page 76, col. 2, parag. 2, lines 1-5). Critical steps must be included for enablement. In claim 160, the method isn't shown to reprogram, and DNA replication is not clearly a part of reprogramming. In claim 162, if the intention is to produce a clone, then the enucleated cell and the nucleus need to be from the same mammalian species for term development.

The specification only teaches one type of cell, an MII oocyte, which has the capability of reprogramming the nucleus. For successful reprogramming, the art taught at the time of filing that the donor nucleus, in a nuclear transfer method needs to be exposed

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to MII cytoplasm (Kono, page 76, col. 2, parag. 2, lines 1-5 and Fluka, page 849, col. 2, parag. 3, lines 4-8). MFP is the active agent in the MII cytoplasm that contributes to reprogramming. While, reprogramming has not been clearly shown in the present case, the purpose of the incubation steps is for reprogramming. Thus, as the MII oocyte is the only cell known to contain sufficient levels of MFP to contribute to reprogramming, and the specification discloses no other cells containing sufficient MFP to reprogram, the claims are enabled only for MII oocyte cytoplasm. Further, it is not clear if the CSF or activating egg cytoplasms from species different from that of the nucleus will provide sufficient MFP and other factors to give successful reprogramming and activation. It is known that with the more traditional nuclear transfer methods where donor nuclei were transferred into oocytes of a different species than the donor nuclei, the development of term-cloned animals is unpredictable (Dinnyes, page 82, col. 2, lines 8-10 and lines 15-20).

The declaration by Alexander D. Baguisi describes the production of cloned mice from a somatic cell by incubation of donor nuclei in the presence of MII oocyte cytoplasm followed by incubation in the presence of activating cytoplasm. While the data presented demonstrates that the methods result in cloned mice, the discussion does not present any details of the method. There is no discussion of the source of the eggs. Further, the method described by Mr. Baguisi used both nuclei incubation with MII oocyte cytoplasm and activating egg cytoplasm. The invention of claims 157 and 160-162 do not require both incubations. Thus the declaration is of a different scope than these claims.

Applicant argues that nuclear transfer was a well-worked out procedure at the time of filing. Applicant argues that the guidance in the specification is sufficient for enablement. These arguments are not persuasive.

For the reasons given above the full scope of applicant's claimed invention is not enabled. Evidence from the relevant art has been provided to support the rejection. The

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question of enablement does not hinge only on whether or not nuclear transfer was a well-worked out methodology at the time of filing. Enablement requires that applicant's contribution to the art of nuclear transfer be capable of implementation by the artisan at the time of filing. It is argued and supported that for the full breadth, this is not current situation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 163 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 163 is confusing in step "b" as it states to treat a pretreated nucleus to produce a pretreated nucleus.

The claims are free of the prior art. At the time of filing, the prior art did not teach or suggest methods for reprogramming a non-dividing nucleus by contacting the nucleus with a cystostatic factor-containing cytoplasm of a cell in meiotic metaphase II, a method of reprogramming a somatic cell nucleus for transplantation into an egg by contacting a nucleus with a cystostatic factor-containing cytoplasm of a cell in meiotic metaphase II prior to activating the nucleus and transplanting the nucleus into an enucleated egg recipient or a method for in vitro activation of a non-dividing nucleus by pretreating an isolate somatic cell nucleus with a cytostatic factor containing cytoplasm and contacting this nucleus with an activating egg cytoplasm.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
April 2, 2003